C5 within 20-30 minutes.

REMARKS

Claims 2, 5-6, 8-20, 23-25 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite as to the word "manipulating". Claims 1-25 are rejected under 25 U.S.C. § 103(a) as being unpatentable over Ekenberg (USPN. 6,218,531) in view of Proudnikov et al. (Nucleic Acids Research 24(22): 4535-4532, 1996).

Reconsideration of the application is requested in light of the foregoing amendments. Independent claim 1 has been amended to recited a radical-mediated labeling process. Support for this added limitation is found throughout the specification, and specifically on page 12, lines 8-9. Independent claims 1, 2, 5, 9-10, and 13 have been amended by replacing "manipulating" with labeling, per the Examiner's suggestion.

Claim 26 has been added to recite a two-buffer, two column process for fractionating and labeling DNA and RNA. Support for this new independent claim is found throughout the specification, and specifically in FIG. 1B, and on page 10, under subheading "RNA/DNA Isolation and Fractionation Detail."

Neither Art of Record Anticipates or Suggests Radical-Driven Chemistry

Claims 1-25 are rejected under 25 U.S.C. § 103(a) as being unpatentable over Ekenberg (USPN. 6,218,531) in view of Proudnikov et al. (Nucleic Acids Research 24(22): 4535-4532, 1996). Applicant submit that in light of the foregoing amendments and the following arguments (including the co-inventor's declaration under 37 C.F.R. 1.132), Proudnikov and Ekenberg are not applicable art.

First, the two pieces of cited art teach away from each other. Proudnikov labels DNA in a column, whereas Ekenberg destroys DNA. Proudnikov labels RNA outside a column, whereas Ekenberg isolates RNA isolation within a column.

Specifically, utilizing the chemistry of Ekenberg (e.g., its reliance of DNase) in Proudnikov will destroy the later's objective of isolating labeling DNA, inasmuch as

DNase destroys DNA. As noted in the attached 1.132 Declaration, the removal of DNA is crucial to enhance Ekenberg's hybridization signal. Only RNA is fractionated in Ekenberg, with DNA treated as detritus. (See last two lines of Ekenberg's Abstract, and also Column 6, lines 45-53. Column 7, lines 30-32, Column 8, line 4-6.) By disclosing various means of destroying DNA or treating the same as detritus, Ekenberg teaches away from Proudnikov's objective of isolating DNA for later manipulation.

Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination. ACS Hospital Systems Inc., v. Montefiore Hospital, 732 F. 2d 1572. Proudnikov deals with labeling RNA and DNA. Ekenberg destroys DNA in the process of purifying RNA. In light of the foregoing, Applicants submit that the posited combination is impermissible hindsight. Withdrawal of the §103 rejection and allowance of claims 1-25 is respectfully solicited.

Assuming *in arguendo* that the Ekenberg-Proudnikov combination is appropriate, Applicants submit that the §103 art is inapplicable inasmuch as neither piece of art suggests radical-based chemistry. In fact, and as stated in the accompanying Part 1.132 Affidavit, the inherent nature of the radical-mediated reactions utilized in the present invention (as originally recited in claims 5, 9, 10, and 13 and as now recited in claims 1 and 2) is vastly different from the chemistry employed in Proudnikov and Ekenberg.

The use of free radicals in the present invention results in the high speed of the method, ***20 minutes***, as opposed to the requisite ***ten hours*** in Proudnikov. (See Proudnikov's Section entitled "Fragmentation of depurinated DNA with ethylenediamine and its fluorescent labeling in solution or in a column" starting on page 4536, second column through page 4537, first column.)

Lastly as to Proudnikov, it is noteworthy that *only DNA* is labeled in a column. (See page 4541, "Conclusions" section of Proudnikov.) Any manipulation of RNA in Proudnikov is done in solution. (See page 4537, "Fluorescent labeling..." sections of Proudnikov.) No method of labeling RNA in a column is suggested by Proudnikov.

As to Ekenberg, no radical chemistry is employed there, either. Rather, adsorption of RNA to silica supports (an ionic interaction) is utilized merely to isolate the RNA from detritus. As noted supra, that detritus includes DNA.

Also, neither Ekenberg nor Proudnikov suggest the use of a two buffer process, as recited in claims 9, 10 and 13, and newly added claim 26. Rather, and as stated by the Examiner on page 4, line 4 of the Official Action, the references requires several buffers, thereby adding to the complexity and total time to complete their processes.

Lastly, neither Ekenberg nor Proudnikov anticipate or suggest the use of anaerobic radical-based chemistry environs to label DNA and RNA, as recited in claim 8. This is because no purposeful steps are undertaken in the references to remove oxygen. To otherwise assert that the references suggest anaerobic conditions without even a mention in the references of aerobic or anaerobic conditions is impermissible hindsight.

The use of anaerobic conditions in the present invention led to unexpected results. The inventors found that, at least for Op-Cu oxidation protocols, a 15 percent increase in hybridization signal was realized when anaerobic conditions were utilized (see original specification, page 14, lines 10-12). Because anaerobic conditions lead to a substantial increase in the hybridization signal in the instant invention, and because none of the art of record even suggests aerobic or anaerobic environs, Applicant submits that the recitation if anaerobic conditions is patentable over said art.

In light of the foregoing, Applicant submits that the 103 rejections based on"Ekenberg and Proudnikov are obviated. Withdrawal of the rejection and allowance of claims 1-25 is respectfully requested.

Reconsideration of FINAL
Designation Requested

Applicants request that the "Final" designation of the latest Official Action be rescinded. For the first time, claims 2, 5-7, 9-10, and 12-19 are rejected based on prior art , and that prior art is first disclosed in the latest Official Action. Previously, the Examiner indicated allowance of said claims would be forthcoming if they were rewritten

(which applicant did) to include limitations of base claims.

During a July 24, 2002 phone call, the Examiner indicated that she would revisit her decision to impose a "Final" rejection.

An earnest attempt has been made hereby to respond to the §§103 and 112 rejections contained in the June 3, 2002 Official Action. It is submitted that all remaining claims are of proper form and scope for allowance. If the Examiner feels that a telephonic interview would expedite allowance of this application, she is respectfully urged to contact the undersigned. Allowance of claims 1-25 and newly added claims 26-27 is respectfully solicited.

Respectfully submitted,

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